Society for Menstrual Cycle Research
POSITION STATEMENT ON THE WOMEN'S HEALTH INITIATIVE AND RANDOMIZED CONTROLLED TRIAL DATA ON "HRT"

The Society for Menstrual Cycle Research (SMCR) is a multi-disciplinary feminist organization promoting accurate and woman-centered science relating to women's reproductive lives**.** In keeping with its holistic approach to the study of women's health research, the Board of Directors presents for the record its formal response regarding the findings of the NIH Women's Health Initiative Estrogen Plus Progestin Arm and randomized controlled trial data. This statement is centered on three important issues:

1. The findings from the WHI Estrogen plus Progestin trial provide outstanding Level 1 evidence in support of the Society's position that menopause is a normal phase of all women's lives and not an estrogen deficiency state that requires hormone "replacement" to prevent serious chronic diseases.
2. The WHI findings when analyzed against the backdrop of previous observational data on menopausal women's risks for cardiovascular disease suggests that a large proportion of the risks for heart attack and stroke can be attenuated by positive lifestyles.
3. Because the WHI trial did not address the perimenopausal years, more longitudinal research is needed to document younger women's health and experiences across the menopausal transition (perimenopause) in multicultural populations. More than ever, funding for the longitudinal, multi-ethnic NIA *Study of Women Across the Nation* (SWAN) needs to be maintained. More research is also needed concerning the etiology of and safer management for hot flashes/night sweats and other changes that are distressing for some women during the menopausal transition and following menopause.

Each of these major points is discussed in more detail below.-

1. WHI results confirm that menopause carries few risks for serious disease.

The results of the largest-ever randomized double blind placebo-controlled trial of Estrogen Plus Progestin showed that-healthy women on hormone therapy experienced significantly more serious diseases during the five years of this trial than did women on the placebo (1). These risks included an excess of blood clots (increased 211%), cardiovascular disease (increased by 29%), breast cancer (increased 26%) and strokes (increased by 41%). Although the absolute numbers of women experiencing these serious health conditions was small rates exceeded the predetermined acceptable threshold of risk for health promotion interventions set by the NIH Data Safety and Monitoring Board, resulting in the early termination of the estrogen plus progestin treatment arm. No increased risk is acceptable in treatment of a normal phase of life in healthy women.

The Society for Menstrual Cycle Research has always endorsed a holistic approach to the study of women's health problems and conditions**.** Current members of the SMCR Board of Directors, while acting as individual scientists (2-4) have questioned the belief that hormone therapy is effective for heart disease and that menopause is a deficiency state (5). At its 14th biennial meeting in June, 2001, a year before any WHI results were available, members of the Society for Menstrual Cycle Research urged a change in language and attitudes related to estrogen and progestin therapy. The SMCR adopted a resolution stating: "Whereas menopause is a normal phase of every woman's life and not

an estrogen deficiency condition . . .the term 'Hormone Replacement Therapy (HRT)' should no longer be used."

2. WHI highlights the key role that lifestyle plays in heart disease prevention

Observational, epidemiological studies of thousands of women have repeatedly shown that estrogen plus progestin use is associated with a decreased risk for coronary heart disease that averages approximately 30-50% (6). However, the participants in these studies who took hormone therapy were self-selected and healthier than those who did not ("the healthy cohort bias"). They were more likely to be of normal weight, physically active, and less likely to have abnormal blood cholesterol and lipid levels, high blood pressure or diabetes. In some studies HT users were of higher educational or socioeconomic status or had better access to medical care. HT users who continued on therapy were adherent to taking it. This "compliance bias" has been shown to be associated with better health even in those assigned to placebo treatments (7).

The results of the WHI E plus P arm demonstrated that hormone therapy *increased* heart disease risk by 29%. Thus, it could be argued that the healthier lifestyle of self-selected hormone users in previous epidemiological studies was powerful enough to overcome even this increased risk. Together these data imply that menopausal women's risk for heart disease can be decreased by 59-79% through simple healthy behaviors such as regular walking, eating sensibly and not smoking, as well as by obtaining appropriate treatment for high blood pressure, abnormal lipids or diabetes.

WHI is not alone in showing no net benefit with hormone therapy—a meta-analysis of randomized controlled trial results in over 20,000 women for up to 4.9 years showed negative health outcomes exceed positive in one of 230 women ages 50-59 and one of 150 women 60-69 (8).

3. Research on the Menopausal Transition and Hot Flashes is needed

The WHI E plus P arm has documented that *asymptomatic* menopausal women do not need ovarian hormone therapy. However, a portion of women are highly symptomatic in the years after menopause and during the sometimes long and hormonally chaotic menopausal transition (9-12). The NIA-funded Study of Women Across the Nation (SWAN) has accomplished a major task in enrolling and evaluating the health of midlife women from many ethnic backgrounds (13). However, important prospective work still lies ahead. Key scientific questions about the experiences in perimenopause must be answered through the continuation and appropriate funding of SWAN.

In response to media reports of the WHI findings, many women have abruptly discontinued hormone therapy, while others have changed regimens or stopped the progestin component. It is important that these self-weaning practices and their health consequences be assessed.

The WHI findings have also magnified the need for randomized, double-blinded clinical trials of therapies for the symptomatic menopausal transition. Many untested herbal, dietary supplement and other alternative therapies are being used to manage night sweats and hot flash symptoms (collectively called vasomotor symptoms, VMS). There is growing evidence that VMS may not be temporary benign or "nuisance" experiences but rather have been linked to increased risks for osteoporosis, sleep disturbances (with associated musculoskeletal disabilities and possible cardiovascular risks) as well metabolic changes such as insulin resistance. For breast cancer patients being treated with tamoxifen

or other hot flash-inducing chemotherapies, VMS can be more severe and debilitating than with spontaneous menopause. The Society believes that much more research support should be devoted to the study of the efficacy and safety of non-hormonal and lifestyle interventions. There is encouraging evidence that some strategies such as paced respiration (14) and Mind Body Therapy (15) decrease VMS significantly more than placebo. Many pharmaceutical alternatives are either costly, have serious side effects or both.

In summary, more research is needed to understand the physiological and experiential changes of women during the menopausal transition. Some women are highly symptomatic. More research is also needed especially to understand the physiology and treatment of VMS in general, and in particular in the subset of women with breast cancer.

Draft written by Jerilynn C. Prior (2002/10, revised 2003/06) for the Society for Menstrual Cycle Research with revisions by and approval of the SMCR at their semi-annual business meeting, June, 2003. Shortened by Nancy Reame and edited by JCP 2003-09-29). Approved by the Board of Directors of SMCR October 6, 2003.

More information on the Society for Menstrual Cycle Research website: www.psu.edu/SMCR.

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